Translation

PATENT COOPERATION TRE



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

1.	<u></u> `		
Applicant's or agent's file refere	FOR FURTHER	ACTION	See Form PCT/IPEA/416
International application No.		date (day/month/year)	Priority date (day/month/year)
PCT/JP2003/01325	9 16 October 2	003 (16.10.2003)	16 October 2002 (16.10.2002)
International Patent Classificatio C12Q 1/60, 1/26, 1/3	n (IPC) or national classification 2, 1/44, G01N 33/92, C07J 1/0	and IPC	
Applicant		1	
	KYOWA ME	DEX CO., LTD.	
This report is the internal Authority under Article	tional preliminary examination re 35 and transmitted to the applican	eport, established by this according to Article 3	International Preliminary Examining 6.
2. This REPORT consists	of a total of8 shee	ts including this cover	heet
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· ·	pplicant and to the International 1	· :	sheets as follower
aliu/0i	of the description, claims and/or sheets containing rectifications a histrative Instructions).	drawings which have be authorized by this Authori	een amended and are the basis of this report onty (see Rule 70.16 and Section 607 of the
Deyon	u die disclosure in the internation	out which this Authority nal application as filed,	considers contain an amendment that goes as indicated in item 4 of Box No. I and the
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	cations relating to the following i	tems:	· .
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Box No. III No	n-establishment of opinion with a	egard to novelty, invent	ive step and industrial applicability
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Box No. V Re		5(2) with regard to nove	ity, inventive step or industrial applicability;
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Date of submission of the deman	d	Date of completion of	f this report
14 May 2004	(14.05.2004)	10 No	vember 2004 (10.11.2004)
Name and mailing address of the	IPEA/JP	Authorized officer	
Facsimile No.		Telephone No.	
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

national application No.
PCT/JP2003/013259

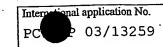
Box N	0. I	Basis of the report	
1. Wit	h regard erwise in	to the language, this report is based on the international application in the adicated under this item.	language in which it was filed, unless
	This whic	report is based on translations from the original language into the follow h is language of a translation furnished for the purpose of:	ring language,
		international search (under Rules 12.3 and 23.1(b))	
		publication of the international application (under Rule 12.4)	•
		international preliminary examination (under Rules 55.2 and/or 55.3)	
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2. With furn. and	are not	to the elements of the international application, this report is based of the receiving Office in response to an invitation under Article 14 are referenced to this report):	n (replacement sheets which have been rred to in this report as "originally filed"
		ternational application as originally filed/furnished	
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	a seque	nce listing and/or any related table(s) - see Supplemental Box Relating to S	
		so Supplemental Box Relating to S	equence Listing.
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٠. []	Ine am	endments have resulted in the cancellation of:	
	ti	ne description, pages	
	U ti	ne claims, Nos.	
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rm PCT	VIPEA/4	109 (Box No. I) (January 2004)	

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

national	application No).

		PCT/JP2003/013259
Box No. IV	Lack of unity of invention	
1. 🔀 In	response to the invitation to restrict or pay additional fees the applicant has:	
· 🗌	restricted the claims.	
	paid additional fees.	•
	paid additional fees under protest.	
	neither restricted nor paid additional fees.	
2. This	Authority found that the requirement of unity of invention is not complied we invite the applicant to restrict or pay additional feet.	with and chara accombing to Dula 60 1
	-pp additional lees.	
3. This Autho	ority considers that the requirement of unity of invention in accordance with I	Rules 13.1, 13.2 and 13.3 is
comp	olied with.	
	omplied with for the following reasons:	
See	supplemental sheet	
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	y, this report has been established in respect of the following parts of the inte	emational application:
⊠ al	ll parts.	
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT



Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

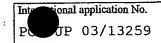
Continuation of: IV. 3.

The inventions set forth in claims 1-10, 12-23 and 25-39 are a group of inventions which address the problem of offering an improved method for simple and accurate measurement of high-density lipoprotein-bound cholesterol, and measurement reagents and kits for the purpose thereof.

By contrast, the inventions set forth in claims 11, 24 and 40-42 are a group of inventions which address the problem of offering compounds described in claim 41.

The two groups of inventions address different problems; therefore, these groups of inventions do not constitute a group of inventions so linked as to form a single general inventive concept.

INTERNATIONAL PACLIMINARY EXAMINATION REPORT



v.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industria	l applicability;
	citations and explanations supporting such statement	. :

Statement			
Novelty (N)	Claims	2,8-11,15,21-24,26-31,37-42	YES
	Claims	1,3-7,12-14,16-20,25,32-36	NO
Inventive step (IS)	Claims	11, 24, 40-42	YES
	Claims	1-10, 12-23, 25-39	NO
Industrial applicability (IA)	Claims	1-42	YES
	Claims		NO.

2. Citations and explanations

Document 1: JP 08-116996 A (Toyobo Co., Ltd.), 14 May 1996

Document 2: WO 97/40376 Al (Iatron Lab. Inc.), 30 October 1997

Document 3: JP 11-009300 A (Iatron Lab. Inc.), 19 January 1999

Document 4: WO 95/24502 Al (Kyowa Medex Co., Ltd.), 14
September 1995

1. The inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are not novel and do not involve an inventive step in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 1 discloses a method for measuring highdensity lipoprotein (HDL) cholesterol characterized in
that the specimen to be tested is reacted with cholesterol
ester hydrolase and (chemically modified) cholesterol
oxidase in an aqueous medium containing a bile acid
derivative having an anionic surfactant action (such as
dehydrocholic acid), and the hydrogen peroxide produced is
measured, and also discloses reagents (a kit) for
measuring high-density lipoprotein (HDL) cholesterol which
contain reagents used in said method of measurement, with

said reagents comprising a first reagent and a second reagent, wherein the cholesterol ester hydrolase and the bile acid derivative are contained in the first reagent, the cholesterol oxidase or cholesterol dehydrogenase is contained in the second reagent, and the reagent for measuring hydrogen peroxide is contained in the first reagent or the second reagent.

Therefore, the inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are substantially the same as the inventions disclosed in document 1.

2. Claims 2, 8-10, 15, 21-23, 26-31 and 37-39 do not involve an inventive step in the light in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 2 (see especially claims 1 and 6 and the section on background art in the detailed description of the invention) discloses reagents containing a bile acid or salt thereof, albumin, a non-ionic surfactant, cholesterol ester hydrolase, cholesterol oxidase and a reagent for measuring hydrogen peroxide, as reagents specific for the measurement of high-density lipoprotein (HDL) cholesterol (kit), and indicates that an anionic bile acid derivative such as taurocholic acid or glycocholic acid can be used as the bile acid; it also discloses a method for specific measurement of highdensity lipoprotein (HDL) cholesterol using said reagents wherein the cholesterol ester hydrolase, cholesterol oxidase and bile acid (derivative) are brought into contact with the specimen in the presence of albumin, and indicates that by this method, namely bringing the test specimen into contact with the enzymes in the presence of albumin, it is possible to inhibit reaction between the

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enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen while reaction between the enzymes and HDL-cholesterol proceeds unimpeded.

It was well known in the art at the time of filing the present application that in general in order to measure high-density lipoprotein (HDL) cholesterol reliably, conditions in which there is as nearly as possible no reaction of the enzymes with LDL cholesterol and VLDL cholesterol present in the specimen (inhibition) are desirable.

Given this a person skilled in the art could easily conceive of applying the invention disclosed in document 2, and bring the enzymes and the specimen into contact in the presence of albumin, in the method for measuring high-density lipoprotein (HDL) cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, applying the aforementioned commonly known fact so as to ensure the aforementioned conditions, namely to inhibit reaction between the enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen, while allowing the reaction between the enzymes and HDL-cholesterol to proceed unimpeded, with the object of accurate measurement of HDL cholesterol.

In addition, document 3 discloses the possibility of using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethylammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, as a bile acid derivative used in a specific method for measuring cholesterol.

Given this, using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethyl-ammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, disclosed

in document 3 as a bile acid derivative used in a specific method for measuring cholesterol, in the method for measuring HDL-cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, also does not involve any special difficulty.

3. The inventions set forth in claims 11, 24 and 40-42 are not disclosed in any of documents 1-4 above, cited in the international search report, and are novel and involve an inventive step.